REMARKS

The Office Action of June 3, 2009 presents the examination of claims 1-10. The present paper cancels claim 10, which is an informal "omnibus" claim. Remaining claims 1-9 are herein amended. All amendments presented are of a formal nature to conform the claims to US claiming practices. No new matter is introduced by any amendment.

Objections to the specification and claims

The Examiner objects to the specification and claims first on the basis that certain trademarks are recited in the specification without proper attribution, and second because occasionally the term "SEQ ID NO:" is incorrectly formatted. A substitute specification, in both "clean" and "track changes" versions is provided that addresses these concerns, and corrects grammatical errors. No new matter has been added. The claims are also amended above to make appropriate corrections.

Claims 3-8 are also objected to for use of the indefinite article at the beginning of these dependent claims. Claims 3-8 are appropriately amended above.

Rejections under 35 USC § 101

Claim 1 is rejected under 35 USC § 101 as reciting non-statutory subject matter; the Examiner asserts that the claimed oligonucleotides should be described as "isolated" so as to reflect the hand of man in the claim.

Such amendment is made above. However, the Examiner should consider that the subject matter was originally described as an "oligonucleotide" having a very short sequence. The Examiner has presented no basis for asserting that such is a naturally occurring product. Applicants' Representative points this out merely to caution the Examiner to carefully consider the facts presented by the application, and not to base her examination only upon doctrine.

Rejections under 35 USC § 112, second paragraph

Claims 1-10 are rejected under 35 USC § 112, second paragraph, as allegedly being indefinite.

In particular, claims 1-8 are said to lack antecedent basis for the phrases, "the banding pattern of the amplified fragments" and "the target region from the DNA of step (a)". Claims 1-8 have been amended to correct this deficiency.

Claims 1-9 are said to be confusing for the recitation "novel oligonucleotide primers having SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO: 4" because the Examiner cannot determine if a single primer including all four sequences is used, or if a plurality of primers having one of the four sequences is used.

Applicants submit that this phrase is not indefinite. First, the phrase includes the word "primers", clearly indicating a plurality of oligonucleotides, and the word "fragments" indicating a plurality of products, which would be obtained by use of a plurality of primers. Second, the specification working examples make quite clear that the four different oligonucleotide primers are used together in a single, multiplexed PCR reaction. See, e.g. page 17, at lines 21 and following.

In any event, the claims are amended to clearly recite that each primer has a different sequence selected from among SEQ ID NOS: 1-4. Furthermore, the claims now clearly recite that each oligonucleotide is one consisting essentially of the recited sequence. Thus, the claimed polynucleotide may include additional nucleotides at either end so long as the additional nucleotides do not interfere with the essential utility of the claimed oligonucleotide as a primer for amplification of *Leishmania* kinesin genes so as to be able to generate products having distinct separation patterns for VL and PKDL causing strains.

Claim 10 is rejected as not reciting any active method steps. Claim 10 is canceled as being an informal omnibus claim.

Thus, the rejections of claims 1-10 under 35 USC § 112, second paragraph are all overcome.

Rejection over prior art

Claims 1-10 are rejected under 35 USC § 103(a) as being unpatentable over Salotra '182, Reed WO '331 and Belli (1998). This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants submit that the Examiner fails to establish *prima facie* obviousness of the claimed invention. In particular, the combined references fail to disclose or suggest at least one element of the claimed invention and also fail to establish an expectation of success in making the present invention.

The Examiner cites Salotra '182 for description of detection of *Leishmania* by PCR. The Examiner admits that Salotra '182 does not provide any suggestion of the particular primers having the sequences of SEQ ID NOS: 1, 2, 3 or 4 as presently claimed. Thus, the Examiner adds Reed WO '331 for disclosure of the primer sequences.

The Examiner's assertion that Reed WO '331 discloses the particular primer sequences SEQ ID NOS: 1-4 of the instant application is incorrect; the Examiner appears to have been misled by the manner in which her search results have been presented. SEQ ID NO: 2 of Reed WO '331 is a nucleotide sequence of a gene (or mRNA) from *L. chagasi* that is 3319 nucleotides long. Of this sequence, the Examiner presents only the individual 17-mers identified by the search algorithm as matching the claimed primer sequence.

Applicants submit that the selection of the particular 17-mer sequences of SEQ ID NOS: 1-4 of the instant invention from among the nearly infinite genus of 17-mers encompassed by the 3319 nucleotide sequence of Reed WO '331 is not *prima facie* obvious. The Examiner points to no disclosure within any of the cited references that guides the skilled artisan to the selection of the particular sequences recited in the present claims, and thus this element of the present invention is not suggested by the references, but rather only by Applicants' present disclosure. Thus, the instant claims are not *prima facie* obvious over the combination of Solotra, Reed and Belli. *See, e.g., In re Baird*, 29 USPQ2d 1550 (Fed. Cir. 1994).

Furthermore, the combined cited references do not establish any reasonable expectation of success in making the present invention. Applicants submit that the present invention provides tools and methods using them for distinguishing between strains of *Leishmania* that cause visceral disease (VL) and strains that cause cutaneous disease (PKDL).

None of the cited references address this problem. Salotra is directed to detection of cutaneous disease-causing strains of *L. donovanii* only (note the title and abstract), with some passing mention of *L. tropica* and *L. major* as not being detected by their assay (note para

[0056]). Salotra provides tools for detecting *Leishmania,* but does not disclose any way to differentiate strains that cause VL from those that cause PKDL. Reed is directed to detection of *Leishmania* species generally, without regard to species or strain distinction, by use of antibodies that are specific for a repeat portion of the kinesin protein that is conserved among species. See, e.g., the description at page 5 of the antigen detected by Reed, and especially that the repeat sequence is one conserved between *L. chugasi* and *L. donovanii*. Thus, Reed fails to differentiate between strains of *Leishmania* that cause VL and those that cause PKDL. Belli (1998) discloses only the detection of *L. braziliensis* by PCR. The Examiner might take due note that no different PCR amplification results are different among the various samples shown in the paper, and thus Belli also fails to distinguish strains of *Leishmania* that cause VL from those that cause PKDL.

In contrast, the present invention provides a primers and a method for using them that allows a clinician not only to detect *Leishmania* infection, but also to distinguish the strain present in a sample so as to accurately diagnose whether it is one that causes visceral or cutaneous disease. In this regard, the Examiner might note the results shown in Figure 1 and described at pp. 20-21 of the present application (Example 3) wherein samples of VL causing strains are distinguishable from PDKL causing strains on the basis of differences in the separation patterns of the PCR products resulting from use of the primers of the present invention. The present invention is thus able to clearly differentiate infection by strains causing VL from infection by strains causing PKDL. The combination of references cited by the Examiner establishes no reasonable expectation of success in making the present invention to obtain such a result.

For the reasons set forth above, the Examiner fails to establish *prima facie* obviousness of the present invention. Alternatively, the results of the invention as shown in Figure 1 must be taken as unexpected by one of ordinary skill in the art who reads the cited papers. Either way, the instant rejection should be withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D., Reg. No. 36,623, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By _____

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